

APPLICANT: Oxford, et al.  
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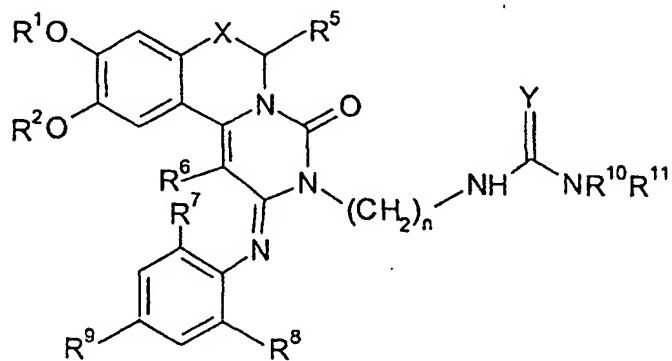
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This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of claims:**

Claims 1-42 (cancelled).

Claim 43 (currently amended): A method for the treatment or prevention of a disease in a mammal where a phosphodiesterase isoenzyme inhibitor and/or a bronchodilator would be expected to be of benefit, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:



I

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wherein

each of R<sup>1</sup> and R<sup>2</sup> independently represents a C<sub>1-6</sub> alkyl or C<sub>2-7</sub> acyl group;  
R<sup>5</sup> represents a hydrogen atom or a C<sub>1-3</sub> alkyl, C<sub>2-3</sub> alkenyl or C<sub>2-3</sub> alkynyl group;  
R<sup>6</sup> represents a hydrogen atom or a C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, amino, C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub>) alkylamino or C<sub>2-7</sub> acylamino group;  
each of R<sup>7</sup> and R<sup>8</sup> independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-7</sub> acyl, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> alkoxy,

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C<sub>3-6</sub> cycloalkyl; and

R<sup>9</sup> represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-7</sub> acyl, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> alkoxy or C<sub>3-6</sub> cycloalkyl group;

X represents OCH<sub>2</sub> or a group CR<sup>3</sup>R<sup>4</sup>, wherein each of R<sup>3</sup> and R<sup>4</sup> independently represents a hydrogen atom or a C<sub>1-3</sub> alkyl group;

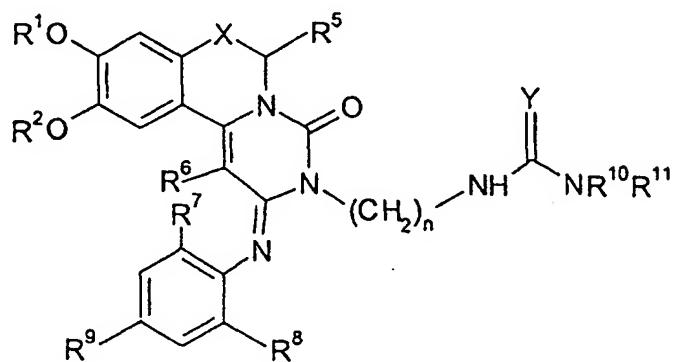
each of R<sup>10</sup> and R<sup>11</sup> independently represents a hydrogen atom, a C<sub>1-3</sub> alkyl, C<sub>3-6</sub> cycloalkyl or phenyl group;

Y represents an oxygen atom or a group CHNO<sub>2</sub>, NCN, NH or NNO<sub>2</sub>;

n is an integer from 2 to 4;

or a salt thereof.

Claim 44 (currently amended): A method for the treatment or prevention of asthma in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:



I

wherein

each of R<sup>1</sup> and R<sup>2</sup> independently represents a C<sub>1-6</sub> alkyl or C<sub>2-7</sub> acyl group;

R<sup>5</sup> represents a hydrogen atom or a C<sub>1-3</sub> alkyl, C<sub>2-3</sub> alkenyl or C<sub>2-3</sub> alkynyl group;

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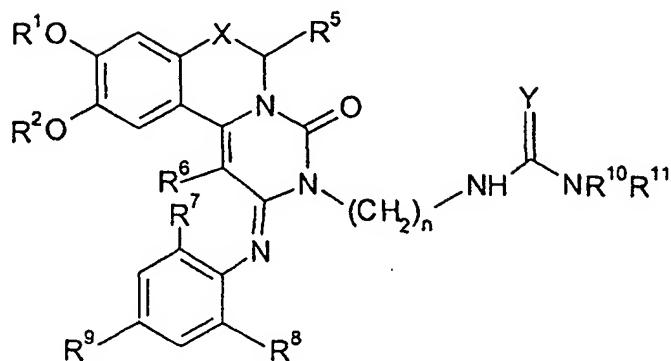
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R<sup>6</sup> represents a hydrogen atom or a C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, amino, C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub>) alkylamino or C<sub>2-7</sub> acylamino group;  
each of R<sup>7</sup> and R<sup>8</sup> independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-7</sub> acyl, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> alkoxy, C<sub>3-6</sub> cycloalkyl; and  
R<sup>9</sup> represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-7</sub> acyl, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> alkoxy or C<sub>3-6</sub> cycloalkyl group;  
X represents OCH<sub>2</sub> or a group CR<sup>3</sup>R<sup>4</sup>, wherein each of R<sup>3</sup> and R<sup>4</sup> independently represents a hydrogen atom or a C<sub>1-3</sub> alkyl group;  
each of R<sup>10</sup> and R<sup>11</sup> independently represents a hydrogen atom, a C<sub>1-3</sub> alkyl, C<sub>3-6</sub> cycloalkyl or phenyl group;  
Y represents an oxygen atom or a group CHNO<sub>2</sub>, NCN, NH or NNO<sub>2</sub>;  
n is an integer from 2 to 4;  
or a salt thereof.

Claim 45 (currently amended): A method for the treatment or prevention of chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:

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I

wherein

each of  $R^1$  and  $R^2$  independently represents a  $C_{1-6}$  alkyl or  $C_{2-7}$  acyl group;  
 $R^5$  represents a hydrogen atom or a  $C_{1-3}$  alkyl,  $C_{2-3}$  alkenyl or  $C_{2-3}$  alkynyl group;  
 $R^6$  represents a hydrogen atom or a  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, amino,  $C_{1-6}$  alkylamino, di( $C_{1-6}$ ) alkylamino or  $C_{2-7}$  acylamino group;  
each of  $R^7$  and  $R^8$  independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{2-7}$  acyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxy,  $C_{3-6}$  cycloalkyl; and  
 $R^9$  represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{2-7}$  acyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxy or  $C_{3-6}$  cycloalkyl group;  
 $X$  represents  $OCH_2$  or a group  $CR^3R^4$ , wherein each of  $R^3$  and  $R^4$  independently represents a hydrogen atom or a  $C_{1-3}$  alkyl group;  
each of  $R^{10}$  and  $R^{11}$  independently represents a hydrogen atom, a  $C_{1-3}$  alkyl,  $C_{3-6}$  cycloalkyl or phenyl group;  
 $Y$  represents an oxygen atom or a group  $CHNO_2$ ,  $NCN$ ,  $NH$  or  $NNO_2$ ;  
 $n$  is an integer from 2 to 4;

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or a salt thereof.

Claim 46 (currently amended): A method as claimed in any of claims 43, 44 or 45, wherein the compound is as defined in any of claims 1 to 15 independently or in any compatible combination:

each of R<sup>1</sup> and R<sup>2</sup> represents a C<sub>1-6</sub> alkyl;

R<sup>1</sup> and R<sup>2</sup> are the same as each other;

each of R<sup>3</sup> and R<sup>4</sup> represents a hydrogen atom;

R<sup>5</sup> represents a hydrogen atom;

R<sup>6</sup> represents a hydrogen atom;

each of R<sup>7</sup> and R<sup>8</sup> represents a C<sub>1-6</sub> alkyl;

R<sup>7</sup> and R<sup>8</sup> are the same as each other;

R<sup>9</sup> represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group CHNO<sub>2</sub>; and

n is 2.

Claim 47 (currently amended): A method as claimed in any of claims 43 to ~~46~~ 45, wherein the compound is administered by aerosol.

Claim 48 (currently amended): A method as claimed in any of claims 43 to ~~47~~ 45, wherein the animal is a human.

Claims 49-50 (cancelled).

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Claim 51 (new): A method as claimed in any of claims 43 to 45, wherein each of R<sup>1</sup> and R<sup>2</sup> represents a C<sub>1-4</sub> alkyl group; and each of R<sup>7</sup> and R<sup>8</sup> represents a methyl, ethyl or isopropyl group.

Claim 52.(new): A method as claimed in any of claims 43 to 45, wherein the compound of general formula I is selected from the group consisting of:

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(N-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[N-(N'-isopropylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[N-[1-(N'-methyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3- [N-[1-(N'-isopropyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[N-[1-(N', N'-dimethyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[N-(N'-phenylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-2-one;  
9, 10-Dimethoxy-3-[2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
9,10-Dimethoxy-3-[N-(N'-nitro)-2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
3-[N-(N'-Cyclohexylcarbamoyl)-2-aminoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;  
3-(N-Carbamoyl-2-aminoethyl)-9,10-dimethoxy-2-(2-methylphenylimino)- 3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one;

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3-(*N*-Carbamoyl-2-aminoethyl)-2-(2,6-diisopropylphenylimino)-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;  
3-(*N*-Carbamoyl-4-aminobutyl)-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)- 3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one; and  
3-[*N*-(*N'*-Cyano-*N*"-methyl)-2-guanidinoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one.